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EXHIBIT A



GL Bischem (Stanghai) Ltd 古年年代 (上述) 非国金司

Breduct Specification

Name: **DMT-CI**

Category: N-Protecting Reagents

Product Data Sheet

Product Name

DMT-CI;

4,4'-Dimethoxytrityl chloride;

4,4'-Dimethoxytriphenylmethyl chloride

40615-36-9

Molecular Formula

CAS No.

C21H19CIO2

Molecular Weight

338.8

Appearance

Light pink color powder

Purity (HPLC)

98% min.

Melting Point

120-125 °C (dec.)

TLC Analysis

One spot

300 MHz ¹H NMR Spectrum (CDCl₃)

Consistent

Loss on Drying

< 0.5%

Solubility Test (In Pyridine)

Clear solution with 1g/10ml

Solvent of Recrystallization

Benzene, Hexanes

Use Test

Passed

EXHIBIT B

PROTECTIVE GROUPS IN ORGANIC SYNTHESIS

Second Edition

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7

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The Upjohn Company



A WILEY-INTERSCIENCE PUBLICATION

JOHN WILEY & SONS, INC.

New York / Chichester / Brisbane / Toronto / Singapore

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Uhrary of Congress Cataloging in Publication Dates

Orces, Theodors W., 1931-

Protective groups in organic symbols (Theodon W. Grezze and Peter G. M. Wats.—2nd ed.

ledufer index.

19EN 0-471-62301-6

1. Organic compounds—Synthesia. 2. Protective groups (Chemistry) L Work, Peter O. M.

QDQ62,C665 1991 ST2-420

8645708 B

Printed in the United States of America

M9876

PREFACE TO THE SECOND EDITION

groups and many new methods of introduction or removal of known protective erences have been sedded. Most of the information from the first edition has been age reactions have been replaced by a single line of conditions, sometimes with explanatory comments, especially regarding selectivity. Some of the new latermation has been obtained from Online Searches of Chemical Abstracts, which have tective groups only if that word appears in the title of the article. References are Since publication of the first edition of this book in 1981, many new protective limitations. For example, Chemical Abstracts indexes a review article about progroups have been developed: 206 new groups and approximately 1500 new reftchined. To conserve space, generic structures used to describe Formation/Cleavcomplete through 1989. Some references, from more widely circularing journals. ue included for 1990.

mines because their chemical properties are sufficiently different to affect the chemistry of protection and deprotection. The Reactivity Chans in Chapter 8 are Two new sections on the protection for indoles, imidazoles, and pyrroles, and protection for the amide -NH are included. They are separated from the regular identical to those in the first edition. The chart number appears beside the name of each protective group when it is first discussed.

isms, Spencer Knapp, and Toltra Fuknyama for many references on amine and A number of people must be thanked for their contributions and help in conpleting this project. I am grateful to Gordon Bundy, who loaned me this card file, which provided many references that the computer failed to find, and to Bob Wilunide protection. I thank Theo Greene who checked and rechecked the manuscript or spelling and consistency and for the herculesa task of checking all the refermoes to make sure my 3s and 8s and 7s and 9s were not interchanged, all without

PROTECTION FOR THE HYDROXYL GROUP, INCLUDING 1,2- AND 1,8-DICKS. 얺

Et, AlCI, CH, CI, 3 min, 70-85 % yield. 19 This method was used to remove the trityl group from various protected deaxyribamodeorides. The TBDPS group is stable to these conditions.

13. Troh, Meoh, 25°, 5 h.20

14. BF3·E40, HSCH2CH2SH, 80% yiekd.²¹

Na, NN₃. ²² Benzyl groups are also removed under these conditions.

ZaBr₂, McOH, 100% yield.²³

57. a-Naphthyldiphenylmethyl Ether: RO-C(Pb)z-a-C₁₀H, (Chart 1)

OE group in nucleosides. It is prepared from a-naphthyldiphenylmethyl chloride p-methoxyphenyldiphenylmethyl other can be cleaved with acid in the presence of in pyridiue (65% yield), and cleaved selectively in the presence of a p-methoxyphenyldiphenylmethyl ether with sodium anthracenide, a (TRP, 97% yield). The The a-naphilyldipheaylmethyl ether was prepared to protect, selectively, the 5'-

58. p-Methoxyphenyldiphenylmethyl Riber (MMTrOR): P-MeOC, H, (Ph), C-OR (Chart 1) 59. Di(p-methoxyphenyl)phenylmethyl Ether (DMTrOR): (p-MeOC,H.), Ph.C.-OR 60. Tri(p-methoxyphenyt)methyl Ether (TMTrOR): (p-MeOC,H,),C-OR

These were originally prepared by Khorana²⁵ as selective protective groups for the 5'-OH of nucleosides and nucleotides. They were designed to be more acid-labile removal of the trityl group. Introduction of p-methoxy groups increases the rate of hydrolysis by about one order of magnitude for each p-methoxy substituent. For S'-protected utidine derivatives in 80% AcOH, 20°, the time for hydrolysis was than the trityl group because depurimention is often a problem in the acid-catalyzed

as follows:

(P-MeOC,H.), (Ph), COR

n = 0, m = 3,48 h

n = 1, m = 2, 2h

R = 2, M = 1, 15 min

 $\kappa = 3$, m = 0, 1 min

oligouncleosides. The monomethoxy derivative has been used for the selective derivatives have been used extensively in the preparation of eligomed conides and The trimethoxy derivative is too labile for most applications, but the mono and diprotection of a primary allylic alcohol over a secundary allylic alcohol (MIMTr, Pyr, - 10°). 26

orchoxy derivative can be cleaved with sodium naphthaleoide in HMPA (90% In practice the various trityl derivatives are cleaved with acid, but the monoyield). 23 It is not cleaved by sodium authmoenide, used to cleave a-amphibyldipheaylanethyl ethers.24

A solution of 3% CCI,CO,H in 95.5 CH3NO,/MeOH is recommended for removal of the DMTr group from the 5'-OH of decaynihonacleatides because at reduced levels of deputitation compared to CL3OO, HICH, CL3, PhSO, HIMEOHY CH2,Cl3, and ZaB5, ICH3NO2.

61. 4-(4'-Bromaphetacyloxyphenyl)diphenylnethyl Effer: P-(P-BrC,H,C(O)CH,O)C,H,(Ph),C-OR

by reductive cleavings (Zd/AcOH) of the piccarryl other to the p-hydroxyphenylderivative is prepared from the corresponding triarylmethyl chloride, and is cheaved This group was developed for protection of the 5'-OH group in medeosides. The diplem/lmethyl ether followed by acidic hydrolysis with formic seid. 29

62. 4,4",4"..Trit(4,5-dichlorophthallmidophenyAmethyl.Ether (CPTr-OR);

It is introduced with CPIVBr/AgNOs/DMR (15 min) in 80-96% yield and can be removed by ammonia followed by 0.01 M HCl or 80% AcOH. 30 It can also be The CPT's group was developed for the protection of the S'-OH of attornactensides. removed with hydrazine and acetic acid. 31

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